

Amended Claims

1.(original) An isolated nucleic acid molecule comprising the nucleotide sequence disclosed in SEQ ID NO: 1.

2.(cancelled)

3.(original) An isolated nucleic acid molecule according to Claim 1 wherein said nucleotide sequence is present in cDNA.

4.(original) An isolated nucleic acid molecule encoding the amino acid sequence described in SEQ ID NO:2.

5. (new) An expression vector comprising a nucleic acid sequence encoding a amino acid sequence drawn from the group consisting of SEQ ID NO: 2.

6.(new) The expression vector of claim 5 wherein said nucleic acid sequence is that of SEQ ID NO:1.

7.(new) A host cell comprising the expression vector of claim 5.

8.(new) The host cell of claim 7 wherein the nucleic acid sequence is that of SEQ ID NO:1.

RESPONSE

I. Status of the Claims

Claim 2 has been cancelled entirely without prejudice and without disclaimer. New claims 5-8 have been added to better claim the present invention. As a result, claims 1, 3-8 are presently pending in the case.

II. Support for the Claims

New claims 5 and 6 has been added to more clearly claim aspects of the invention. Claims 5 and 6 find support throughout the specification, sequence listing and claims as originally filed, with particular support being found at least at or about page 14 lines, 13-19 and in original SEQ ID NOS: 1 and 2.

New claims 7 and 8 has been added to more clearly claim aspects of the invention. Claims 7 and 8 find support throughout the specification, sequence listing and claims as originally filed, with particular support being found at least at or about page 14 lines, 19-25 and in original SEQ ID NOS: 1 and 2.

As new claims 5-8 are fully supported by the specification, sequence listing and claims as originally filed, they do not constitute new matter. Entry is therefore respectfully requested.

III. Objection

The Action objects to the abstract of the application as being non-descriptive. Applicants point out that numerous issued U.S. Patents have an abstract identical to the present abstract. Specifically, Applicants direct the Examiner's attention to issued U.S. Patent Nos. 6,433,153, 6,441,153, 6,441,154, 6,444,456 and 6,448,388. As issued U.S. Patents are presumed to meet all necessary PTO requirements, Applicants respectfully submit that the present abstract must also meet all necessary PTO requirements.

Applicants request that as the objection has been overcome, this objection be withdrawn.

IV. Rejection of All Claims Under 35 U.S.C. § 101

The Action rejects claims under 35 U.S.C. § 101, allegedly because the claimed invention lacks support by either a specific and substantial asserted utility or a well established utility. Applicants respectfully traverse.

The Action discounts many of the numerous utilities described in the specification for the sequences of the present invention based on the position that while credible, these utilities are not specific or substantial. While Applicants in no way agree with the Examiner's arguments, Applicants have chosen to expand on only a few of the utilities as only one is required.

Applicants respectfully submit that the legal test for utility involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

In *In re Brana*, (34 USPQ2d 1436 (Fed. Cir. 1995), "Brana"), the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of

further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted. In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is “undue”, not “experimentation”. *In re Angstadt and Griffin*, 190 USPQ 214 (C.C.P.A. 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Even under the newly installed utility guidelines, Applicants note that MPEP 2107 (II)(B)(1) states:

- (1) If the applicant has asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a “specific and substantial utility”) and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility. (MPEP 2107 (II)(B)(1))

Applicants would first like to invite the Examiner’s attention to the fact that a sequence sharing greater than 99% identity at the amino acid level with a large portion of SEQ ID NO:2 of the present invention is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as “phospholipase B1 [*Homo sapiens*] (GenBank accession number XP_371487, alignment and information provided as **Exhibit A**). Applicants note that phospholipase B1 is also known to the art as PLB1.

Phospholipases are known to be enzymes that convert phospholipids into fatty acids and other lipophilic substances. There are four major classes, termed A, B, C and D. The function of phospholipase B has been characterized and its function is known to those of skill in the art, as exemplified by many scientific publications, for example: “Identification of Functional Domains of Rat Intestinal Phospholipase B/Lipase” (Takemori, *et al.*, *J Biol Chem.* **273**(4):2222-

2231:1998, provided as **Exhibit B**), "The phospholipase B homolog Plb1 is a mediator of osmotic stress response and of nutrient-dependent repression of sexual differentiation in the fission yeast *Schizosaccharomyces pombe*" (Yang, *et al.*, *J Biol Chem.* **273**(4):2222-2231:1998, abstract provided as **Exhibit C**), and "Identification of phospholipase B from *Dicyostelium* reveals a new lipase family present in mammals, flies and nematodes, but not yeast" (Morgan, *et al.*, *Biochem J.* *Epub ahead of print*, Jun 14 2004, abstract provided as **Exhibit D**). Therefore, clearly, there can be no question that the sequences of the present invention encode a novel slightly longer isoform of human phospholipase B that has a specific, substantial and well established utility.

The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this GenBank annotation and the described publications, there can be no question that those skilled in the art would clearly believe that the molecule encoded by the sequences of the present invention have specific, substantial and well established utility. As such, the scientific evidence clearly establishes that Applicants have described an invention whose utility is in full compliance with the provisions of 35 U.S.C. § 101, and therefore Applicants respectfully request withdrawal of the rejection.

The Action suggests that Applicants could not have made an assertion regarding utility as there are no working examples, indicating a need for such information are misplaced. It has long been established that "there is no statutory requirement for the disclosure of a specific example". *In re Gay*, 135 USPQ 311 (C.C.P.A. 1962).

In the specification, Applicants asserted that the sequences of the present invention share sequence similarity with other animal lipases, and particularly phospholipase B (page 2, lines 2-3). Applicants respectfully submit that those of skill in the art would recognize these statements as an assertion that the sequences of the present invention do indeed encode human phospholipase B isoforms. Applicants' assertion is that the sequences of the present invention encode novel variants of human phospholipase B. As novel variants these sequences differ slightly from previously identified sequences encoding human phospholipase B, but certainly as expected, share structural similarity with sequences known to encode animal lipases and particularly phospholipase B. These statements in the specification assert that the sequences of the present invention and phospholipase B share a similarity in structure, a similarity in function and a recognized similarity in biological function. This would be accepted by those of skill in the art, as it is generally recognized that there is a structure-function relationship. Absent any evidence

of record that the described human phospholipase B isoform somehow fails to function as does phospholipase B, the Examiner has failed to meet his/her burden of establishing that the Applicants' assertion of protein function is not credible. Accordingly, the Examiner is respectfully requested to either provide evidence that substantially and specifically refutes the Applicants' asserted function/utility, or withdraw the rejection. Clearly, the sequences of the present invention have patentable utility and pending rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph should be withdrawn.

If, somehow, the above arguments were not deemed sufficient, it should also be noted that the rejection of the present invention due to lack of patentable utility also runs contrary to Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when there is no reason to doubt the asserted utility of a full length sequence that has a similarity score of 95% to a protein having a known function. In the Analysis portion of Example 10 it states that "Based on applicant's disclosure and the results of the PTO search, there is no reason to doubt the assertion that SEQ ID NO:2 encodes a DNA ligase. Further DNA ligases have a well-established use in the molecular biology art based on this class of proteins ability to ligate DNA.Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed..... Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made."

In the present case, clearly evidence supports Applicants' assertions that the sequences of the present invention encode novel isoforms of human phospholipase B, a class of proteins for which there is a well established utility that is recognized by those of skill in the art. The present case is identical to that presented in Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55). In the present case it is clear that the sequences of the present invention encode novel isoforms of human phospholipase B with greater than a 95% identity to a protein having a known function (phospholipase B), as asserted in the specification. However, even if, *arguendo*, Applicants had failed to assert this utility, according to the guidelines "Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed... Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be

made”(emphasis added). Thus, the present rejection of the presently claimed invention under a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph utility rejection should not have been made and should be withdrawn.

In addition to the above presented evidence countering the Actions suggestion that Applicants knew of no specific use at the time the application was filed that would permit an immediate use by the public of a disclosed nucleic acid sequence. However, the specification details a number of uses for the presently claimed polynucleotide sequences, among these were, use in diagnostic assays such as forensic analysis (see, for example, the specification at page 3, line 9 and page 11, line 28), identification of protein coding sequence and identification of exon splice junctions (see, for example, the specification at page 3, line 5, and page 11, lines 13-18), in mapping the sequences to a specific region of a human chromosome (see, for example, the specification at page 3, line 3 and page 17, lines 8-10), and in assessing gene expression patterns, particularly using a high throughput “chip” format (see, for example, the specification at page 6, line 3 through page 8).

While only one utility for the sequences of the present invention is required, Applicants submit the following additional examples of specific, substantial and real world utility. The specification describes polymorphisms identified in the claimed sequences (page 17, lines 11-14) a “C/T polymorphism was identified at the sequence region represented by nucleotide position 3953 of SEQ ID NO:1, which can result in an ala or val at corresponding amino acid position 1318 of SEQ ID NO:2.”

Naturally occurring genetic polymorphisms such as those described in the present specification are both the basis of, and critical to, *inter alia*, forensic genetic analysis and genetic analysis intended to resolve issues of identity and paternity. These utilities are clearly real world, given that the results of identity and paternal analysis often have great emotional and substantial economic impact. This is not a throw away utility, rather it sounds like a very substantial and real world utility. What could be more substantial and real world than the loss of an individual’s freedom through incarceration and in some cases even the loss of life through execution? Yet forensic analysis based on identified polymorphisms is often used to convict or acquit in many cases. Both paternal and forensic genetic analysis is based on the use of identified polymorphisms. This is a well known and generally accepted by those of skill in the art, who would readily recognize the utility and value of any identified polymorphism. Without identified polymorphisms, one would not be able to carry out such forensic or paternal analyses. The present

application has identified just such essential polymorphisms within the sequences of the present invention which identify variants of the human phospholipase B.

As such polymorphisms are the basis for forensic analysis, paternity identification and population biology studies, which are undoubtedly “real world” utilities, the present sequences must in themselves be useful. In and of themselves each of these polymorphisms, including the silent ones, has significant and specific utility, the specificity of this utility is only amplified by the presence of so many polymorphisms that can arise in various combinations. It is also important to note that the presence of more useful polymorphic markers for such analysis would not mean that the present sequences lack utility.

Applicants respectfully point out that those of skill in the art would readily recognize that the presently described polymorphisms, exactly as they were described in the specification as originally filed, are useful in forensic analysis, population biology and paternity analysis to specifically identify individual members of the human population based on the presence or absence of the described polymorphism. Simply because the use of these polymorphic markers will necessarily provide additional information on the percentage of particular subpopulations that contain one or more of these polymorphic markers does not mean that “additional research” is needed in order for these markers as they are presently described in the instant specification to be of use to forensic science. Without further experimentation those of skill in the art would recognize the utility of the identified polymorphisms and how the asserted markers can distinguish 50% of the population in the worst case scenario. Thus the presence or the absence of a particular specific polymorphism is sufficient for use in the proposed utilities. Applicants provide the following detailed explanation. Those of skill in the art would recognize that in the worst case, least useful situation, a marker would be present in half of a population and absent from the other half. Therefore the probability of an individual having such a marker would be 1 in 2 or 50%. Using the forensic analysis scenario for example, the analysis will have removed 50% of the possible suspects from the list, as either the suspect has the identified polymorphism or not. However, if a polymorphism were present in only say 10% of the population, the probability of an individual having such a polymorphic marker would be 1 in 10 (10%) and 90% of suspects could be eliminated from investigation or prosecution based on the presence or absence of the polymorphism. Clearly eliminating 90% of the suspects is better than eliminating 50% of the suspects. That said, eliminating 50% or half of the suspects on a list is without question very useful to any investigator. To reiterate, using the polymorphic markers as described in the

specification as originally filed will definitely distinguish members of a population from one another. In the worst case scenario, each of these markers are useful to distinguish 50% of the population (in other words, the marker being present in half of the population). The ability to eliminate 50% of the population from a forensic analysis clearly is a real world, practical utility. Therefore, any allegation that the use of the presently described polymorphic markers is only potentially useful would be completely without merit, and would not support the alleged lack of utility.

Should the Examiner incorrectly conclude that any human nucleic acid sequence that contains a naturally occurring polymorphism can be used in forensic analysis, in human paternity determinations or human population migration determinations, such utilities are generic and therefore lack substantial and specific utility. First, Applicants submit that until a specific polymorphic marker is actually described it has very limited utility in forensic analysis. Put another way, simply because there is a possibility, even a significant likelihood, that a particular nucleic acid sequence will contain a polymorphism and thus be useful in forensic analysis, until such a specific polymorphism is actually identified and described, such a likelihood is meaningless. The present case contains identified polymorphisms that occur in a novel isoform of human phospholipase B. Should the Examiner consider using the information presented for the first time by Applicants in the instant specification as hindsight verification that the presently claimed sequence would be expected to have polymorphic markers. Such a hindsight analysis based on Applicants discovery would not be proper.

Alternatively, any assumption that since any sequence containing a naturally occurring polymorphism can be used such utilities are generic and therefore lack substantial and specific utility may represent a confusion between the requirement for a specific utility, which is the proper standard for utility under 35 U.S.C. § 101, with a requirement for a unique utility. The relevant case law cited by Applicants makes it abundantly clear that the presence of other or even more useful polymorphic markers for forensic analysis does not mean that the present sequences lack a specific utility. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; “*Carl Zeiss*”):

An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: “[T]he fact that an invention has only limited utility and is only operable in certain applications is

not grounds for finding a lack of utility.” *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Importantly, the holding in the *Carl Zeiss* case is mandatory legal authority that essentially controls the outcome of the present appeal. This case, and particularly the cited quote, directly rebuts any such argument. Furthermore, the requirement for a unique utility is clearly not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer and bacterial or viral infections, just to name a few particular examples, because examples of each of these have already been described and patented. All batteries have the exact same utility - specifically, to provide power. All automobile tires have the exact same utility - specifically, for use on automobiles. All golf balls and golf clubs have the exact same utility - specifically, use in the game of golf. All cancer treatments have the exact same utility - specifically, to treat cancer. All anti-infectious agents have the exact same broader utility - specifically, to treat infections. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Although the above discussions are believed to be dispositive of the utility issue in this case, Applicants would like to further direct the Examiner’s attention to the parts of the specification that describe the use of sequences in a gene chip format to provide a high throughput analysis of the relevant cellular “transcriptome”, including assessing temporal and tissue specific gene expression patterns, particularly using a high throughput “chip” format (specification at or about page 6, line 3 through page 8).

Evidence of the “real world” substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example:

Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company, Rosetta Inpharmatics, was viewed to have such “real world” value that it was acquired by large pharmaceutical company, Merck & Co., for substantial sums of money (net equity value of the transaction was \$620 million). The “real world” substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, *Science* 291:1304, presented as **Exhibit E**). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, *Science* 291:1153, presented as **Exhibit F**). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years). The sequences of the present invention have particularly specific utility in DNA gene chip based analysis as they have been identified to contain several coding region single nucleotide polymorphisms (cSNPs), thus increasing their utility in DNA gene chip based analysis.

DNA chips clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776 (**Exhibits G-L**; copies of issued U.S. Patents not provided pursuant to current United States Patent and Trademark Office policy). Accordingly, the present sequence has a specific utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, like the present sequences, which encode a novel human phospholipase B isoform, have identified polymorphisms and a characterized tissue expression pattern, must have utility. The sequences of the present invention which encode the human phospholipase B isoform, provide specific markers for a human genome (see also chromosome mapping discussion below and information provided in the specification at page 3, lines 1-3 and page 17, lines 7-10, that indicate that this protein is encoded on human chromosome 2). Thus, those skilled in the art would instantly recognize that the sequences of the present invention would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips, as the specification details. Accordingly, the present sequence has a specific utility in such DNA chip applications. Clearly,

compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequence encoding human phospholipase B isoform must also be useful.

The Examiner is further requested to reconsider that, given the huge expense of the drug discovery process, even negative information obtained using these specific markers of expression of a human phospholipase B isoform provides very specific markers for the human genome and have great “real world” practical utility. Knowing that a given gene is not expressed in medically relevant tissue provides an informative finding of great value to industry by allowing for the more efficient deployment of expensive drug discovery resources. Such practical considerations are equally applicable to the scientific community in general, in that time and resources are not wasted chasing what are essentially scientific dead-ends (from the perspective of medical relevance). Clearly, compositions that enhance the utility of DNA gene chips, such as the presently claimed sequences encoding a human phospholipase B isoform, must in themselves be useful. Moreover, the presently described human phospholipase B isoform sequences provide uniquely specific sequence resources for identifying and quantifying full length transcripts that were encoded by the corresponding human genomic locus. Accordingly, there can be no question that the described sequences provide an exquisitely specific utility for analyzing gene expression. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Further evidence of utility of the presently claimed polynucleotide, although only one is needed to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), is the specific utility the present nucleotide sequence has in determining the genomic structure of the corresponding human chromosome, for example mapping the protein encoding regions as described in the specification. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome 2 containing the gene encoding the given polynucleotide which encodes a human phospholipase B isoform, a utility not shared by virtually any other nucleic acid sequence. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

The Action discounts Applicants' assertion regarding the use of the presently claimed polynucleotides for gene mapping and determining chromosome structure again based on the position that such a use would allegedly be generic and therefore fail to represent a specific and substantial utility. However, as only a minor percentage of the genome actually encodes exons, which in turn encode amino acid sequences, the presently claimed polynucleotide sequence provides biologically validated empirical data (e.g., showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* defines that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The Applicants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence supporting the Applicants' position, the Board is requested to review, for example, section 3 of Venter *et al.* (*supra* at pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article.

Evidence provided in **Exhibit M** supports Applicants' assertions of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome and identification of functionally active intron/exon splice junctions. **Exhibit M** is the result of overlaying the sequence of SEQ ID NO:1 of the present invention and the identified human genomic sequence. By doing this one is readily able to identify the portions of the genome that encode the present invention. If these regions of the genome are non-contiguous, this is indicative of individual exons. The results of such an analysis indicates that the sequence of the present invention is encoded by greater than 56 exons spread non-contiguously along a region of human chromosome 2, (as stated in the specification as filed on page 17, lines 7-10) which is also contained within the BAC clones AC074011.5 and AC093164.6). Thus clearly one would not simply be able to identify the more than 56 distinct protein encoding exons that make up the sequence of the present intention from within the large genomic sequence. Nor, would one be able to map the protein encoding regions identified specifically by the sequences of the present invention without knowing exactly what those specific sequences were. Additionally, it should

be noted that the human phospholipase B is now recognized to map to the same region of human chromosome 2. This further supports Applicant's position that the sequences of the present invention encodes a human phospholipase B isoform encoded on human chromosome 2, as was described in the specification.

In addition, among other things the mapping of the relatively few expressed human genes to a particular chromosome has long been a recognized method of identifying genes associated with particular diseases. Furthermore, the mapping of the human chromosome is a project of such widely recognized importance by those of skill in the art and even lay people, that both the US government and private corporations have dedicated millions of dollars to such a project. One is thus forced to ask, if the mapping of human chromosomes is a throw away utility then why has the US government spent so many taxpayer dollars on this project?

Finally, with full recognition of the fact that all patent applications are examined on their own merits and that the prosecution of one patent does not effect the prosecution of another patent, *In re Wertheim*, 541 F.2d 257, 264, 191 USPQ 90, 97 (CCPA 1976), however the issue at hand is one of whether the fact that patents have issued recognizing the utility of a class of molecules does this confers a statutory precedent of patentability to a broad class of compositions. Thus, there remains a lingering issue regarding due process and equitable treatment under the law.

While Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides; **Exhibits N-P**; copies of issued U.S. Patents not provided pursuant to current United States Patent and Trademark Office policy), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples; **Exhibit Q**; copies of issued U.S. Patents not provided pursuant to current United States

Patent and Trademark Office policy), none of which contain examples of the “real-world” utilities that the Examiner appears to desire. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section IV, below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants agree that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Applicants invention to a different standard of utility appears inconsistent and inequitable, such a judgement being arbitrary and capricious, a violation of due process and equal protection under the law and cannot be maintained.

In light of the evidence presented herewith and for the many compelling reasons described above, it is clear that the present invention encodes a novel human phospholipase B isoform and that the utility of such molecules are specific, substantial and credible and are well-established. Therefore, Applicants submit that the rejection of the pending claims under 35 U.S.C. § 101 has been avoided. Applicants, therefore, respectfully request withdrawal of the pending rejection of claims under 35 U.S.C. § 101.

V. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

The Action also rejects all claims under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as the present invention has been shown to have “a specific, substantial, and credible utility”, as detailed in the preceding section, the rejection under 35 U.S.C. § 112, first paragraph, has been avoided. Applicants therefore request that the rejection of the pending claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

VI. Rejection of Claim 2 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects Claim 2 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. The Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19 USPQ2d 1111 (Fed. Cir. 1991); “*Vas-Cath*”) held that an “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.*” *Vas-Cath*, at 1117, emphasis in original. However, it is important to note that the above finding uses the terms reasonable clarity to those skilled in the art. Further, the Federal Circuit in *In re Gosteli* (10 USPQ2d 1614 (Fed. Cir. 1989); “*Gosteli*”) held:

Although [the applicant] does not have to describe exactly the subject matter claimed, . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

Gosteli at 1618, emphasis added. Additionally, *Utter v. Hiraga* (6 USPQ2d 1709 (Fed. Cir. 1988); “*Utter*”), held “(a) specification may, within the meaning of 35 U.S.C. § 112 ¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses” (*Utter*, at 1714). Therefore, all Applicants must do to comply with 35 U.S.C. § 112, first paragraph, is to convey the invention with reasonable clarity to the skilled artisan.

Further, the Federal Circuit has held that an adequate description of a chemical genus “requires a precise definition, such as by structure, formula, chemical name or physical properties” sufficient to distinguish the genus from other materials. *Fiers v. Sugano*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; “*Fiers*”). *Fiers* goes on to hold that the “application satisfies the written description requirement since it sets forth the . . . nucleotide sequence” (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph.

More recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that

the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Univ. of California v. Eli Lilly and Co.*:

In claims to genetic material ... a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as opposed to the situation set forth in *Univ. of California v. Eli Lilly and Co.* and *Fiers*, the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the sequence itself.

The Action, on page 3, lines 15-16, states that "Regarding claim 2, it is directed to all possible nucleic acid sequences that hybridizes to SEQ ID NO:1..." Applicants respectfully disagree.

Applicants respectfully submit that Claim 2 has two limitations, the first being that molecules which encode the amino acid sequence shown in SEQ ID NO: 2; and the second being hybridization under stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof and covered nucleic acid molecules must meet both conditions, not just one. Applicants submit that the nucleic acid molecules identified by the intersection of both parts of Claim 2, those that encode the amino acid sequence shown in SEQ ID NO: 2; and hybridize under stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof, is a finite and well defined group, which those of skill in the art could easily identify and would

know how to make and use. Therefore, Applicants respectfully submit that the rejection of Claim 2 under 35 U.S.C. § 112, first paragraph, is not proper. However, as Claim 2 has been cancelled entirely without prejudice or disclaimer this rejection has been rendered moot.

VII. Rejection of Claim 2 Under 35 U.S.C. § 102(b)

The Action further rejects Claim 2 under 35 U.S.C. § 102(b) as allegedly being anticipated by Boll, *et al* and Zhu. Once again the Examiner has neglected to recognize that Claim 2 has two limitations, the first being that molecules which encode the amino acid sequence shown in SEQ ID NO: 2; and the second being hybridization under stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof. Even if, *arguedo*, the disclosed sequences would hybridize to SEQ ID NO: 1, they would not be anticipated to encode the amino acid sequence shown in SEQ ID NO: 2 and would therefore not anticipate Claim 2. However, as Claim 2 has been cancelled entirely without prejudice or disclaimer these rejections have also been rendered moot.

VIII. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Nashed have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

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